Extremely dynamic protein systems: Integrating single molecule fluorescence and nuclear magnetic resonance spectroscopy

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Intrinsically disordered proteins (IDPs) lack clearly defined three-dimensional structure and sample many different conformations on a sub-microsecond time scale. These extremely dynamic proteins are highly flexible and easily adaptable to different binding partners, making them important players in many biological processes, often with vital regulatory functions. Their dynamic features and broad range of interaction modes, however, render them difficult to study, and analyzing their complexes often requires integrated approaches.

My group exploits the complementary nature and distance dependence of nuclear magnetic resonance (NMR) and single molecule fluorescence, in particular single molecule Förster Resonance Energy Transfer (FRET), to study the conformational landscape and dynamics of IDPs at molecular resolution. Qualitative and quantitative approaches are undertaken to effectively integrate parameters from both techniques to shed new light onto how IDPs and their interactions with folded proteins regulate and enable various biological processes.

A particular focus of the group lies on the process of clathrin-mediated endocytosis, the major cellular uptake pathway of eukaryotic cells, which exploits a complex network of IDP-driven interactions during its initiation phase. We uncovered a plethora of interactions of various strengths and dynamic features, which we suspect to be responsible for reshaping the interaction network to finally lead to the uptake of a clathrin-coated vesicle.